PAIN® 152 (2011) 123–130

PAIN®

www.elsevier.com/locate/pain

Sad mood increases pain sensitivity upon thermal grill illusion stimulation: Implications for central pain processing

Michael Karl Boettger [a,*,1], Christiane Schwier [b,1], Karl-Jürgen Bär [b]

[a] Institute of Physiology I, University Hospital, Jena, Germany
[b] Department of Psychiatry and Psychotherapy, University Hospital, Jena, Germany

ARTICLE INFO

Article history:
Received 1 March 2010
Received in revised form 18 September 2010
Accepted 4 October 2010

Keywords:
Thermal grill illusion
Pain
Mood induction
Central pain processing
Cold pain thresholds
Heat pain thresholds

ABSTRACT

In different fields of neuroscience research, illusions have successfully been used to unravel underlying mechanisms of stimulus processing. One such illusion existing for the field of pain research is the so-called thermal grill illusion. Here, painful sensations are elicited by interlacing warm and cold bars, with stimulus intensities (temperatures) of these bars being below the respective heat pain or cold pain thresholds. To date, the underlying mechanisms of this phenomenon are not completely understood. There is some agreement, however, that the sensation evoked by this stimulation is generated by central nervous interactions. Therefore, we followed two approaches in this study: firstly, we aimed at developing and validating a water-driven device which might be used in fMRI scanners in future studies – subject to minor adaptations. Secondly, we aimed to interfere with this illusion by induction of a sad mood state, a procedure which is suggested to influence central nervous structures that are also involved in pain processing.

The newly developed device induced thermal grill sensations similar to those reported in the literature. Induction of sad, but not neutral mood states, resulted in higher pain and unpleasantness ratings of the painful illusion. These findings might be of importance for the understanding of pain processing in healthy volunteers, but putatively even more so in patients with major depressive disorder. Moreover, our results might indicate that central nervous structures involved in the affective domain or cognitive domain of pain processing might be involved in the perception of the illusion.

1. Introduction

The phenomenon of a moderately painful and awkward sensation evoked by spatially alternating warm and cold stimuli below the respective pain thresholds has first been described in 1896 [45] and was later called "illusion of pain" or "painful grill illusion". Only recently electrophysiological and psychophysiological methods have been applied to examine putative underlying mechanisms in greater detail. In their landmark paper, Craig and Bushnell [13] could show that nearly all participants perceived the combination of temperatures, that caused warmth or cold feelings when presented on their own, to be painful. In the same study, recordings from the cat spinal cord revealed a dramatically reduced response of thermoreceptive-specific 'COLD' cells in lamina I upon simultaneous warm and cold stimulus presentation, while the response of heat, pinch and cold (HPC) cells was unaltered. However, it remains speculation at which level of sensory processing the painful sensation is actually generated. Besides convergence or inhibitory mechanisms at the spinal level [13,16,21,22], the hypothalamus and various regions of the cortex have been discussed as candidate regions [13,14]. In particular, the anterior cingulate cortex (ACC) has been shown to be activated by grill stimuli in imaging experiments, while the isolated warm and cold stimuli of the grill were not capable of evoking similar activation in the same study [14]. The ACC further appears to be crucially involved in central processing of emotional and motivational aspects of pain such as unpleasantness [14,43]. Due to the nature of the evoked sensation, the thermal grill illusion has in addition been proposed as an experimental model for central pain states [15].

Taken together, a close examination of this phenomenon promises to reveal important insights into central pain processing. Like in other fields of neuroscience, e.g., in the visual system, the application of an illusion bears an enormous potential to uncover underlying physiological and pathophysiological mechanisms [18]. Since a Peltier-element driven generation of different temperatures [11,14] makes an application in functional magnetic resonance imaging (fMRI) scanners impossible, we aimed at

* Corresponding author. Address: Universitätsklinikum Jena, Institut für Physiologie I/Neurophysiologie, Teichgraben 8, 07743 Jena, Germany. Tel.: +49 (0) 3641 938864; fax: +49 (0) 3641 938812.
E-mail address: mkboettger@gmx.de (M.K. Boettger).
[1] These authors contributed equally to this work.

0304-3959/$36.00
doi:10.1016/j.pain.2010.10.003

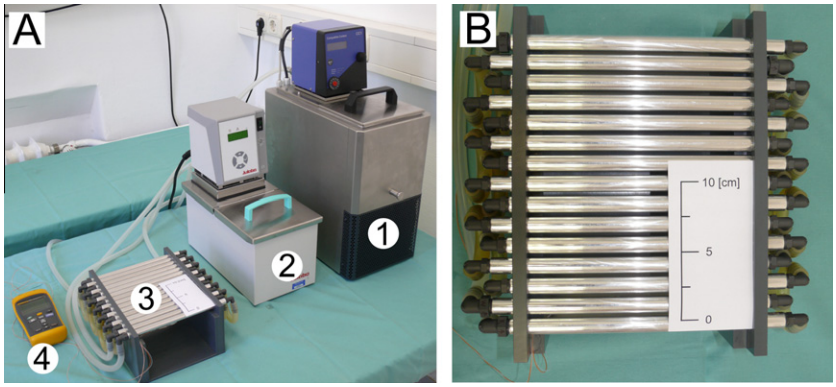

Fig. 1. Experimental setup for eliciting the thermal grill illusion. (A) Water is cooled and heated, respectively, in two thermostats (1, 2) and pumped through every other bar in the grill device (3 and B). At the measuring site where the palm is being placed (3), the temperature is being measured by a digital thermometer (4).

validating a water-driven thermal grill device that can be used in such experiments in an adapted design in future studies. Thus, we obtained basic data and assessed temperature differences at which the alternating stimuli were perceived painful including respective pain ratings and compared these to those described in the literature.

Considering the body of evidence pointing towards a central nervous generation of this pain illusion [14,15,25], we further aimed to interfere with pain processing on the cortical level. We have previously shown that sad mood induction leads to a sensitization to heat pain [46,47]. Therefore, participants were subjected to a modified Velten mood-induction procedure (MIP) to compare sad and neutral emotional states. In both conditions, the painful sensation elicited by the thermal grill was quantified regarding pain intensity and unpleasantness of the sensation applying visual analogue scales (VAS).

2. Materials and methods

2.1. Thermal grill

A thermal grill device was designed according to previous literature [11,13] consisting of 15 tubes with 16 cm length and 10 mm diameter and a distance between tubes of 3 mm (number 3 in Fig. 1A and B). Heating and cooling of these tubes were accomplished by perfusion with either warm or cold water which was regulated to the respective temperatures using thermostats (Huber, Germany; Julabo, Germany, 1 and 2 in Figure 1A). Effective temperatures at the tubes were controlled using a digital thermometer (4 in Figure 1A).

2.2. Subjects

For validation of the water-driven thermal grill (protocol 1, also see Fig. 2A), 26 healthy participants were recruited (for demographic data, see Table 1).

For the investigation of emotional state on the thermal grill perception (protocol 2, Fig. 2B), 32 additional healthy female volunteers between 20 and 28 years of age participated in this study (see Table 1). They were recruited by flyer advertisement and email requests. All participants were right-handed, according to the German version of the Edinburgh Handedness Inventory [34].

Prior to the experiment, participants were asked to complete the Beck Depression Inventory (BDI, [7]), the state-trait-anxiety-inventory (STAI, [40]) and a questionnaire about current clinical symptoms and past medical history.

Potential subjects who presented with one of the following conditions were excluded: any organic origin of pain complaints, chronic pain, any neurological or psychiatric signs or symptoms as assessed by a standardized interview and a clinical examination, current use of analgesic or antidepressant medication, alcohol or substance dependency and use of alcohol within 12 h before the experiment.

For inclusion, all subjects were required to give written informed consent to a protocol approved by the Ethics Committee of the Medical Faculty of the Friedrich-Schiller-University, Jena.

2.3. Experimental design

2.3.1. Protocol 1 (validation of the device, Fig. 2A)

At first, cold and heat pain thresholds (CPT and HPT) were determined consecutively by an ascending method of limits as described previously [4,39]. In brief, a 9 cm^2 contact thermode (TSA-2001; Medoc, Israel) was placed on the palm of both hands one at a time, i.e., the same area at which grill testing was performed later, and temperature was decreased or increased at a rate of 0.5 °C/s (baseline temperature: 32.0 °C; minimal temperature: 0 °C, maximal temperature: 53.0 °C). To determine thermal pain thresholds, participants were asked to follow the written instruction: "When

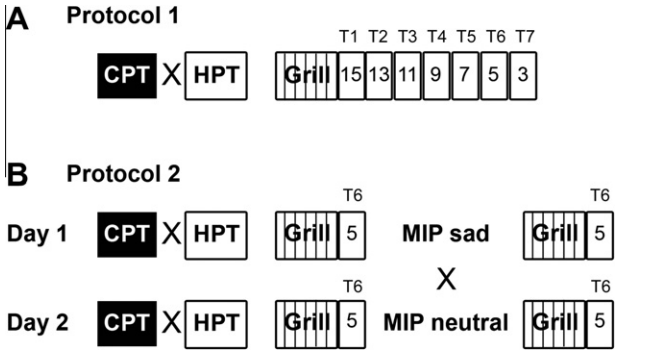

Fig. 2. Protocols for validation (A, protocol 1) and the mood-induction procedure (MIP, B, protocol 2). (A) For validation, cold pain thresholds (CPT) and heat pain thresholds (HPT) were obtained in random order (*X*). From these thresholds, the temperatures applied to the different bars were calculated. In protocol 1, 7 temperature combinations were used (T1–T7). In the first test (T1), cold bars were set 15 °C above CPT, and warm bars to 15 °C below HPT (represented by the numbers displayed). Then, T2–T7 were performed using differences from the respective thresholds of 13, 11, 9, 7, 5 and 3 °C. (B) In order to assess the influence sad mood induction on the thermal grill perception, CPT and HPT were obtained corresponding to protocol 1. Then, pain and unpleasantness ratings were assessed for the grill illusion using a temperature 5 °C above CPT for the cold bars and 5 °C below HPT for the warm bars (according to T6 in protocol 1). Following this, either sad or neutral mood was induced on one of the two testing days and the grill perception was repeated. The order of mood induction (sad or neutral) was randomized across subjects (*X*).